STIC Search Report
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STIC Database Tracking Number: 149332

TO: Kevin Weddington **Location: rem/3a65/3c70** **Art Unit: 1614** **Wednesday, April 13, 2005** **Case Serial Number: 10/633402**	**From: Edward Hart** **Location: Biotech-Chem Library** **REM-1A55** **Phone: 571-272-2512** **edward.hart@uspto.gov**

Search Notes

Examiner Weddington,

Here are the results of the search you requested.

Please feel free to contact me if you have any questions.

Edward Hart

DEM-3670

Access DB# 149332

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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: K. Weddington Examiner # : 68082 Date: 3-30-05
Art Unit: 1614 Phone Number ~~30~~ 272-0587 Serial Number: 10/633,402
Mail Box and Bldg/Room Location: 3A 65 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

A method of ~~pre~~protecting non-mucosal tissue against damage from radiation therapy by administering a composition comprising

1) glutamine

The non-mucosal tissue is selected from

skin

breast tissue

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: _____	NA Sequence (#)_____		STN	_____
Searcher Phone #: _____	AA Sequence (#)_____		Dialog	_____
Searcher Location: _____	Structure (#) _____		Questel/Orbit	_____
Date Searcher Picked Up: _____	Bibliographic _____		Dr.Link	_____
Date Completed: _____	Litigation _____		Lexis/Nexis	_____
Searcher Prep & Review Time: _____	Fulltext _____		Sequence Systems	_____
Clerical Prep Time: _____	Patent Family _____		WWW/Internet	_____
Online Time _____	Other _____		Other (specify)	_____

PTO-1590 (1-2000)

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                E SHINAL C/AU
L14            11 S E4-E5
L15           133 S L10 OR L11 OR L12 OR L13 OR L14
L16             0 S L10 AND L11 AND L12 AND L13 AND L14
L17             1 S L5 AND L15
L18            67 S L2 AND (RADIATION (L) THERAP?)
L19            32 S L18 AND (SKIN OR BREAST OR TISSUE)
L21             3 S L18 AND L19 AND MUCOSAL
L22             0 S L18 AND (NON (L) MUCOSAL (L) TISSUE)
L23             0 S L19 AND (NON (L) MUCOSAL (L) TISSUE)
L24            15 S L18 AND (SKIN OR BREAST (L) TISSUE)

     FILE 'HCAPLUS' ENTERED AT 14:14:12 ON 13 APR 2005

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L24  ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:759809  HCAPLUS
DOCUMENT NUMBER:          141:271543
TITLE:                    Methods of treating and preventing proliferative
                          disease with antiplatelet or anticlotting agent in
                          combination with antineoplastic agent and/or
                          radiation therapy
INVENTOR(S):              Dicker, Adam P.; Burd, Randy; Sidhu, Kulbir
PATENT ASSIGNEE(S):       Technology Center, USA
SOURCE:                   U.S. Pat. Appl. Publ., 16 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2004180812         A1    20040916    US 2003-737360          20031215
PRIORITY APPLN. INFO.:                       US 2002-433471P     P   20021213
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AB The present invention provides methods of treating proliferative disease in a patient (e.g., a mammal such as a human) in need of such treatment, said treatment comprising administering, concurrently or sequentially, an effective amount of (1) an anti-platelet or anti-clotting agent and (2) an anti-neoplastic agent and/or **radiation therapy.** A second method of treatment comprises administering Plavix, also known as clopidogrel, or SR 25909 to a patient in need of such treatment. An addnl. method comprises administering an anti-platelet or anti-clotting agent to an individual at risk for developing proliferative disease. The methods of the present invention are particularly useful for the treatment or prevention of various cancers, especially epithelial cancers, e.g., prostate cancer, lung cancer, breast cancer, colorectal cancer, and pancreatic cancer. In preferred embodiments, the anti-platelet agent is combined with one of the following antineoplastic agents: taxotere, gemcitabine, paclitaxel (Taxol), 5-Fluorouracil (5-FU), cyclophosphamide (Cytoxan), temozolomide, or Vincristine. Treatment of human U87 gliobastoma tumor xenografts in mice with Plavix alone resulted in a 5 day tumor growth delay (TGD). Treatment of the tumors with X-ray **radiation** increased the TGD to 12 days, while treatment with **radiation** and Plavix combined increased the TGD to 16 days (4 days more than **radiation** alone).

IT **133652-38-7**, Reteplase **191588-94-0**, Tenecteplase
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiplatelet or anticlotting agent in combination with antineoplastic agent and/or **radiation therapy** for treating and preventing proliferative disease)

L24 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:681680 HCAPLUS
DOCUMENT NUMBER: 141:200162
TITLE: Mitochondrial malate dehydrogenase DNA fragmentation activator fragment and related conjugated proteins and antibodies for cancer therapy
INVENTOR(S): Wright, Susan C.; Larrick, James W.; Nock, Steffen R.; Wilson, David S.
PATENT ASSIGNEE(S): Palo Alto Institute of Molecular Medicine, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004070012	A2	20040819	WO 2004-US2974	20040202
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004191843	A1	20040930	US 2004-770668	20040202
PRIORITY APPLN. INFO.:			US 2003-444191P P	20030203
			US 2003-460855P P	20030408

AB The invention provides compns. comprising amino acid sequences that have cell killing activity, nucleic acid sequences encoding them, antibodies that specifically bind with them, and methods of using these compns. for increasing and/or reducing cell death, detecting cell death, diagnosing diseases associated with altered cell death, and methods for identifying test agents that alter cell death. More particularly, the invention provides an activator of DNA fragmentation (ADF), a C-terminal fragment of mitochondrial MDH (malate dehydrogenase), which can induce DNA fragmentation by activating nuclease endogenous to normal nuclei. The invention also provides a conjugate comprising a cell death-inducing mol. (such as ADF) and a cell mol.-recognizing compound, and use of said conjugate in killing cancer cells. Specifically, the invention relates that conjugate can be composed of said ADF and/or other mitochondrial/non-mitochondrial cell death-inducing proteins (such as Htra/Omi, apoptosis inducing factor, Smac/DIABLO, EndoG, Nix, Nip3, CIDE-B, gelsolin, Bcl-2, Bax, Bad, Bid, caspase-activated DNase, DNase I or DNase II), and that cell mol.-recognizing compds. can include antibodies or growth factors. In particular embodiments, recombinant ADF proteins, ADF-Ant (antennapedia) and rADF-bFGF, are shown to be cytotoxic to a variety to tumor cell types, and even drug-resistant cancer cell

lines.

IT **742221-52-9**
RL: PRP (Properties)
(unclaimed protein sequence; mitochondrial malate dehydrogenase DNA fragmentation activator fragment and related conjugated proteins and antibodies for cancer therapy)

IT **253328-23-3**
RL: PRP (Properties)
(unclaimed sequence; mitochondrial malate dehydrogenase DNA fragmentation activator fragment and related conjugated proteins and antibodies for cancer therapy)

L24 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:100955 HCAPLUS
DOCUMENT NUMBER: 140:157441
TITLE: Cyclooxygenase- 2 selective inhibitors, compositions and methods of use
INVENTOR(S): Garvey, David S.; Khanapure, Subhash P.; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004010945	A2	20040205	WO 2003-US23605	20030729
WO 2004010945	A3	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004072883	A1	20040415	US 2003-628375	20030729
PRIORITY APPLN. INFO.:			US 2002-398829P	P 20020729

OTHER SOURCE(S): MARPAT 140:157441

AB The invention describes novel cyclooxygenase 2 (COX-2) selective inhibitors and novel compns. comprising at least one cyclooxygenase 2 (COX-2) selective inhibitor, and, optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or at least one therapeutic agent. The invention also provides novel kits comprising at least one COX-2 selective inhibitor, optionally nitrosated and/or nitrosylated, and, optionally, at least one nitric oxide donor, and/or, optionally, at least one therapeutic agent. The novel cyclooxygenase 2 selective inhibitors of the invention can be optionally nitrosated and/or nitrosylated. The invention also provides methods for treating inflammation, pain and fever; for treating and/or improving the gastrointestinal properties of COX-2 selective inhibitors;

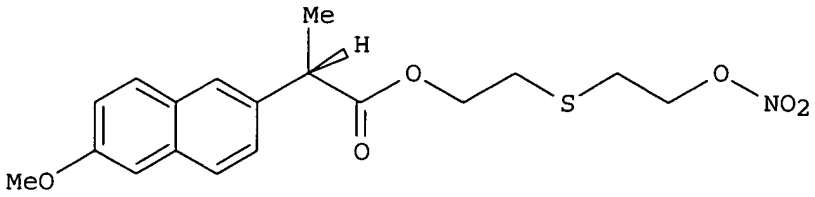
for facilitating wound healing; for treating and/or preventing renal and/or respiratory toxicity; for treating and/or preventing other disorders resulting from elevated levels of cyclooxygenase-2; and for improving the cardiovascular profile of COX-2 selective inhibitors.

IT **56-85-9**, L-Glutamine, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory cyclooxygenase-2 selective inhibitors)

L24 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41217 HCAPLUS
DOCUMENT NUMBER: 140:111135
TITLE: Preparation of nitrosated nonsteroidal antiinflammatory compounds
INVENTOR(S): Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-Jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004004648	A2	20040115	WO 2003-US21026		20030703
WO 2004004648	A3	20041028			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004024057	A1	20040205	US 2003-612014		20030703
PRIORITY APPLN. INFO.:			US 2002-393111P	P	20020703
			US 2002-397979P	P	20020724
			US 2002-418353P	P	20021016
			US 2003-449798P	P	20030226
			US 2003-456182P	P	20030321

OTHER SOURCE(S): MARPAT 140:111135
GI



II

AB Title compds. RnRmHC-CO-X [Rm = H, alkyl; Rn = 4-((thiophen-2-yl)carbonyl)phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH2Cl2, DMAP, EDCI) and treated with Ac2O/HNO3 at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

IT **56-85-9**, Glutamine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of naproxen-derived nitrosated antiinflammatory compds.)

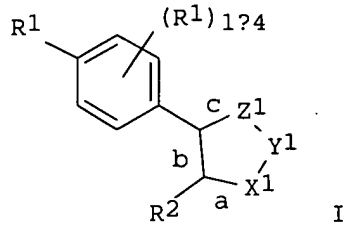
L24 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20441 HCAPLUS
DOCUMENT NUMBER: 140:77147
TITLE: Preparation of optionally nitrosated and/or nitrosylated oxime and/or hydrazone cyclooxygenase-2 selective inhibitors, compositions and methods of use
INVENTOR(S): Garvey, David S.; Ranatunge, Ramani R.; Richardson, Stewart K.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002420	A2	20040108	WO 2003-US20421	20030630
WO 2004002420	A3	20040701		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-392044P P 20020628
OTHER SOURCE(S): MARPAT 140:77147

GI



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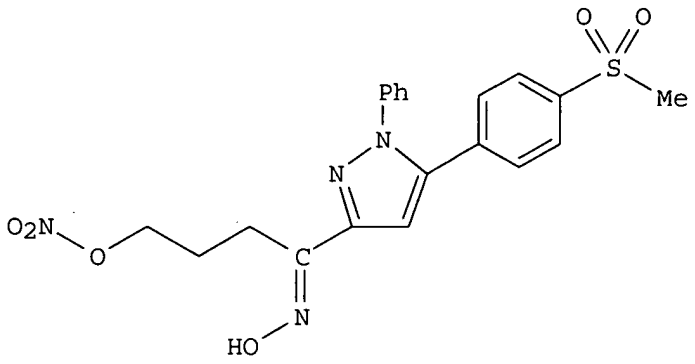

II

AB The invention describes novel cyclooxygenase 2 (COX-2) selective inhibitors having at least one oxime group or hydrazone group optionally nitrosated and/or nitrosylated (one class shown as I; variables defined below; e.g. II; 15 other classes of compds. are also described in the 1st claim) and novel compns. and kits comprising at least one I and optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or at least one therapeutic agent. The invention also provides methods for treating inflammation, pain and fever; for treating and/or improving the gastrointestinal properties of COX-2 selective inhibitors; for facilitating wound healing; for treating and/or preventing renal and/or respiratory toxicity; for treating and/or preventing other disorders resulting from elevated levels of cyclooxygenase-2; and for improving the cardiovascular profile of COX-2 selective inhibitors. Six examples of I were tested for inhibition of COX-1 and COX-2; e.g. 1-[1-cyclohexyl-3-[1-(hydroxyimino)-4-(nitrooxy)butyl]pyrazol-4-yl]-4-(methylsulfonyl)benzene inhibited COX-1 10 % at 100 μM and COX-2 100 % at 10 μM. Although the methods of preparation are not claimed, 6 example prepns. are included. For example, II was prepared in 7 steps (79, 68, 84, 79, 51, 84 and 48 % yields, resp.) starting from di-Me oxalate, NaOMe and 4'-(methylthio)acetophenone in toluene and involving intermediates Me (2Z)-2-hydroxy-4-(4-methylthiophenyl)-4-oxobut-2-enoate, Me 5-(4-methylthiophenyl)-1-phenylpyrazole-3-carboxylate, N-methoxy-N-methyl-5-(4-methylthiophenyl)-1-phenylpyrazole-3-carboxamide, 1-[5-(4-methylthiophenyl)-1-phenylpyrazol-3-yl]-4-(1,1,2,2-tetramethyl-1-silapropoxy)butan-1-one, 4-hydroxy-1-[5-[4-(methylsulfonyl)phenyl]-1-phenylpyrazol-3-yl]butan-1-one, and

1-[5-[4-(methylsulfonyl)phenyl]-1-phenylpyrazol-3-yl]-4-(nitrooxy)butan-1-one. For I: when side b is a double bond, and sides a and c are single bonds, -X1-Y1-Z1- is: -CR4(R5)CR5(R5')CR4(R5)-, -C(O)CR4(R4')CR5(R5')-, -CR4(R4')CR5(R5')C(O)-, -[CR5(R5')]kOC(O)-, etc.; when sides a and c are double bonds and side b is a single bond, -X1-Y1-Z1- is: :CR4OCR5:, :CR4NR3CR5:, :NSCR4:, :CR4SN:, etc. R1 is S(O)2Me, S(O)2NR8(D1), S(O)2N(D1)C(O)CF3, S(O)(NH)NH(D1), S(O)(NH)N(D1)C(O)CF3, P(O)MeNH(D1), P(O)Me2, C(S)NH(D1), S(O)(NH)Me, P(O)MeOD1, or P(O)MeNH(D1); R1' is H, halo, Me, or CH2OH. R2 is lower alkyl, cycloalkyl, mono, di- or trisubstituted Ph or naphthyl, mono, di- or trisubstituted heteroaryl (wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1-3 addnl. N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1-4 addnl. N atoms), benzoheteroaryl, NR10R11, SR11, OR11, R11, alkenyl, alkynyl, unsubstituted, mono, di, tri- or tetrasubstituted cycloalkenyl, mono, di, tri- or tetrasubstituted heterocycloalkyl group of 5-7 members, or a benzoheterocycle, wherein said heterocycloalkyl or benzoheterocycle contains 1 or 2 heteroatoms selected from O, S, or N and, optionally, contains a carbonyl group or a sulfonyl group, styryl, mono or disubstituted styryl, phenylacetylene, mono- or disubstituted phenylacetylene, fluoroalkenyl, mono- or disubstituted bicyclic heteroaryl of 8-10 members, containing 2-5 heteroatoms (wherein at least one heteroatom resides on each ring of said bicyclic heteroaryl, said heteroatoms are each independently O, S and N), K, aryl, arylalkyl, cycloalkylalkyl, -C(O)R11, hydrogen, arylalkenyl, arylalkoxy, alkoxy, aryloxy, cycloalkoxy, arylthio, alkylthio, arylalkylthio, or cycloalkylthio. R3 is hydrogen, haloalkyl (preferably CF3), CN, lower alkyl, [C(Re)(Rf)]p-U-V, K, (un)substituted lower alkyl-Q, lower alkyl-O-lower alkyl-Q, etc., Q, alkylcarbonyl, arylcarbonyl, alkylarylcarbonyl, arylalkylcarbonyl, carboxylic ester, carboxamido, cycloalkyl, mono, di- or trisubstituted Ph or naphthyl, alkenyl, alkynyl, arylalkyl, lower alkyl-OD1, alkoxyalkyl, aminoalkyl, lower alkyl-CO2R10, lower alkyl-C(O)NR10(R10'), heterocyclic alkyl, or heterocyclic ring-C(O)-; with the proviso that one oxime or hydrazone group must be present; addnl. details are given in the claims.

IT **56-85-9**, Glutamine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of optionally nitrosated and/or nitrosylated oxime and/or hydrazone cyclooxygenase-2 selective inhibitors, compns. and methods of use)

L24 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20431 HCAPLUS
DOCUMENT NUMBER: 140:77146
TITLE: Preparation of trisubstituted pyrazole cyclooxygenase-2 selective inhibitors
INVENTOR(S): Bandarage, Upul K.; Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Khanapure, Subhash P.; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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FILE COVERS 1907 - 13 Apr 2005  VOL 142 ISS 16
FILE LAST UPDATED: 12 Apr 2005  (20050412/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L2         71817 S L1
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               E RADIATION
L3        669136 S E3
               E THERAPY
L4        257216 S E3
L5            56 S L2 AND L3 AND L4
               E SKIN/CT
L6        165796 S E3+ALL
               E BREAST
               E BREAST/CT
L7         59269 S E3+ALL
               E TISSUE/CT
L8         55161 S E3+ALL
L9             5 S L5 AND L6 AND L7 AND L8
               E KLINBERG S/AU
               E KLIMBERG S/AU
L10           27 S E4-E6
               E PETIT R/AU
L11           38 S E3
               E PETIT G/AU
L12           58 S E3,E13
               E SHINAL E,AU
               E SHINAL E/AU
L13           10 S E5
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002409	A2	20040108	WO 2003-US19850	20030625
WO 2004002409	A3	20040819		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004053985	A1	20040318	US 2003-603098	20030625
PRIORITY APPLN. INFO.:			US 2002-391769P	P 20020627
			US 2003-454307P	P 20030314

OTHER SOURCE(S): MARPAT 140:77146
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = SO2CH3, SO2NH2; R1' = H, halo, Me, CH2OH; R2 = alkyl, cycloalkyl, aryl, heterocyclic ring; R3 = (un)substituted alkyl, acyl, etc.] are prepared For instance, Me (Z)-2-hydroxy-4-(4-methylthiophenyl)-4-oxobut-2-enoate (preparation given) is reacted with cyclooctylhydrazine trifluoroacetate (preparation given) (MeOH, 70°) to give Me 1-cyclooctyl-5-(4-methylthiophenyl)pyrazole-3-carboxylate. This is reduced (THF, LAH), oxidized to the sulfone (MeOH/H2O, oxone) and reacted with NHO3/Ac2O (CHCl3) to give II. Compds. of the invention exhibit cyclooxygenase 2 (COX-2) selectivity; II exhibits 75% inhibition of COX-2 at 10 μM and 35% inhibition of COX 1 at 100 μM. The invention also provides novel kits comprising at least one COX-2 selective inhibitor, optionally nitrosated and/or nitrosylated and optionally at least one nitric oxide donor and/or optionally at least one therapeutic agent. The novel cyclooxygenase 2 selective inhibitors of the invention can be optionally nitrosated and/or nitrosylated. Therapies are also disclosed that provide methods for: treating inflammation, pain and fever, for improving the gastrointestinal properties of COX-2 selective inhibitors, for facilitating wound healing, etc.

IT **56-85-9**, Glutamine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of trisubstituted pyrazole cyclooxygenase-2 selective inhibitors)

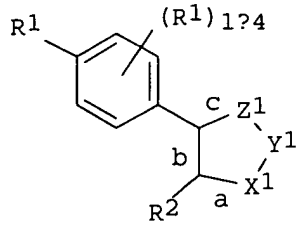
L24 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:20345 HCAPLUS
DOCUMENT NUMBER:	140:77144
TITLE:	Preparation of optionally nitrosated and/or nitrosylated oxime and/or hydrazone cyclooxygenase-2 selective inhibitors, compositions and methods of use
INVENTOR(S):	Ranatunge, Ramani R.; Garvey, David S.; Richardson, Stewart K.
PATENT ASSIGNEE(S):	Nitromed, Inc., USA
SOURCE:	U.S. Pat. Appl. Publ., 74 pp. CODEN: USXXCO

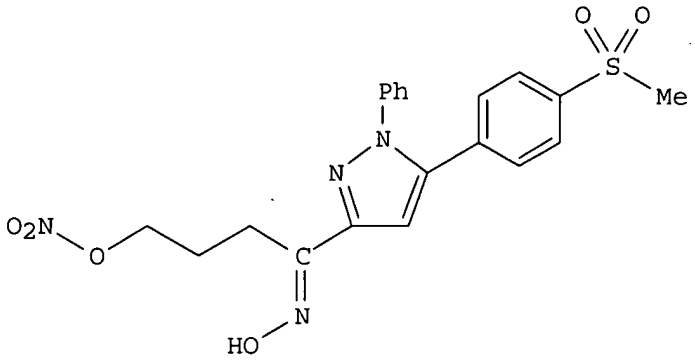
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004006133	A1	20040108	US 2003-608333		20030630
PRIORITY APPLN. INFO.:			US 2002-392044P	P	20020628

OTHER SOURCE(S): MARPAT 140:77144
GI



I



II

AB The invention describes novel cyclooxygenase 2 (COX-2) selective inhibitors having at least one oxime group or hydrazone group optionally nitrosated and/or nitrosylated (one class shown as I; variables defined below; e.g. II; 15 other classes of compds. are also described in the 1st claim) and novel compns. and kits comprising at least one I and optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or at least one therapeutic agent. The invention also provides methods for treating inflammation, pain and fever; for treating and/or improving the gastrointestinal properties of COX-2 selective inhibitors; for facilitating wound healing; for treating and/or preventing renal and/or respiratory toxicity; for treating and/or preventing other disorders resulting from elevated levels of cyclooxygenase-2; and for improving the cardiovascular profile of COX-2 selective inhibitors. Six examples of I were tested for inhibition of COX-1 and COX-2; e.g. 1-[1-cyclohexyl-3-[1-(hydroxyimino)-4-(nitrooxy)butyl]pyrazol-4-yl]-4-(methylsulfonyl)benzene inhibited COX-1 10

% at 100 μM and COX-2 100 % at 10 μM. Although the methods of preparation are not claimed, 6 example prepns. are included. For example, II was prepared in 7 steps (79, 68, 84, 79, 51, 84 and 48 % yields, resp.) starting from di-Me oxalate, NaOMe and 4'-(methylthio)acetophenone in toluene and involving intermediates Me (2Z)-2-hydroxy-4-(4-methylthiophenyl)-4-oxobut-2-enoate, Me 5-(4-methylthiophenyl)-1-phenylpyrazole-3-carboxylate, N-methoxy-N-methyl-5-(4-methylthiophenyl)-1-phenylpyrazole-3-carboxamide, 1-[5-(4-methylthiophenyl)-1-phenylpyrazol-3-yl]-4-(1,1,2,2-tetramethyl-1-silapropoxy)butan-1-one, 4-hydroxy-1-[5-[4-(methylsulfonyl)phenyl]-1-phenylpyrazol-3-yl]butan-1-one, and 1-[5-[4-(methylsulfonyl)phenyl]-1-phenylpyrazol-3-yl]-4-(nitrooxy)butan-1-one. For I: when side b is a double bond, and sides a and c are single bonds, -X1-Y1-Z1- is: -CR4(R5)CR5(R5')CR4(R5)-, -C(O)CR4(R4')CR5(R5')-, -CR4(R4')CR5(R5')C(O)-, -[CR5(R5')]kOC(O)-, etc.; when sides a and c are double bonds and side b is a single bond, -X1-Y1-Z1- is: :CR4OCR5:, :CR4NR3CR5:, :NSCR4:, :CR4SN:, etc. R1 is S(O)2Me, S(O)2NR8(D1), S(O)2N(D1)C(O)CF3, S(O)(NH)NH(D1), S(O)(NH)N(D1)C(O)CF3, P(O)MeNH(D1), P(O)Me2, C(S)NH(D1), S(O)(NH)Me, P(O)MeOD1, or P(O)MeNH(D1); R1' is H, halo, Me, or CH2OH. R2 is lower alkyl, cycloalkyl, mono, di- or trisubstituted Ph or naphthyl, mono, di- or trisubstituted heteroaryl (wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1-3 addnl. N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1-4 addnl. N atoms), benzoheteroaryl, NR10R11, SR11, OR11, R11, alkenyl, alkynyl, unsubstituted, mono, di, tri- or tetrasubstituted cycloalkenyl, mono, di, tri- or tetrasubstituted heterocycloalkyl group of 5-7 members, or a benzoheterocycle, wherein said heterocycloalkyl or benzoheterocycle contains 1 or 2 heteroatoms selected from O, S, or N and, optionally, contains a carbonyl group or a sulfonyl group, styryl, mono or disubstituted styryl, phenylacetylene, mono- or disubstituted phenylacetylene, fluoroalkenyl, mono- or disubstituted bicyclic heteroaryl of 8-10 members, containing 2-5 heteroatoms (wherein at least one heteroatom resides on each ring of said bicyclic heteroaryl, said heteroatoms are each independently O, S and N), K, aryl, arylalkyl, cycloalkylalkyl, -C(O)R11, hydrogen, arylalkenyl, arylalkoxy, alkoxy, aryloxy, cycloalkoxy, arylthio, alkylthio, arylalkylthio, or cycloalkylthio. R3 is hydrogen, haloalkyl (preferably CF3), CN, lower alkyl, [C(Re)(Rf)]p-U-V, K, (un)substituted lower alkyl-Q, lower alkyl-O-lower alkyl-Q, etc., Q, alkylcarbonyl, arylcarbonyl, alkylarylcarbonyl, arylalkylcarbonyl, carboxylic ester, carboxamido, cycloalkyl, mono, di- or trisubstituted Ph or naphthyl, alkenyl, alkynyl, arylalkyl, lower alkyl-OD1, alkoxyalkyl, aminoalkyl, lower alkyl-CO2R10, lower alkyl-C(O)NR10(R10'), heterocyclic alkyl, or heterocyclic ring-C(O)-; with the proviso that one oxime or hydrazone group must be present; addnl. details are given in the claims.

IT **56-85-9**, Glutamine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of optionally nitrosated and/or nitrosylated oxime and/or hydrazone cyclooxygenase-2 selective inhibitors, compns. and methods of use)

L24 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:991031 HCAPLUS
DOCUMENT NUMBER: 140:40889
TITLE: Modified anti-tumor necrosis factor immunoglobulins containing extra constant region Ig domain inserted into its constant region and their therapeutic uses
INVENTOR(S): Scallon, Bernard J.; Cai, Ann; Naso, Michael
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232046	A1	20031218	US 2003-454948	20030605
WO 2003105898	A1	20031224	WO 2003-US17742	20030605

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2002-388896P P 20020614

AB The present invention relates to modified anti-tumor necrosis factor Igs. The modified anti-TNF Igs contains an extra constant region Ig domain inserted into its constant region. The invention also provides vector, host cell and methods for production of the modified anti-TNF Igs. The invention also relates to formulation of modified anti-TNF Igs for therapeutic uses. The invention also relates to uses of modified anti-TNF Igs for treatments of immune disease, cancer and infection.

IT **9023-70-5**, Glutamine synthetase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as selectable marker for expression of Ig; modified anti-tumor necrosis factor Igs containing extra constant region Ig domain inserted into its constant region and their therapeutic uses)

L24 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:358204 HCAPLUS
DOCUMENT NUMBER: 139:111245
TITLE: Phase II study of antineoplaston A10 and AS2-1 in patients with recurrent diffuse intrinsic brain stem glioma. A preliminary report
AUTHOR(S): Burzynski, Stanislaw R.; Lewy, Robert I.; Weaver, Robert A.; Axler, Maxwell L.; Janicki, Tomasz J.; Jurida, Gabor F.; Paszkowiak, Jaroslaw K.; Szymkowski, Barbara G.; Khan, Mohammad I.; Bestak, Mark
CORPORATE SOURCE: Department of Internal Medicine, Burzynski Clinic, Houston, TX, USA
SOURCE: Drugs in R&D (2003), 4(2), 91-101
CODEN: DRDDFD; ISSN: 1174-5886
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twelve title patients received escalating doses of antineoplaston A10 and AS2-1 by i.v. bolus injections. The median duration of treatment was 6 mo and the average dosage of antineoplaston A10 was 11.3 g/kg/day and of antineoplaston AS2-10.4 g/kg/day. Responses were assessed by Gd-enhanced magnetic resonance imaging of the head. Of ten evaluable patients, complete response occurred in two cases, partial response in three, stable disease in three and progressive disease in two. Survival after 2 yr was

33.3%. Currently, of all 12 patients, two (17%) were alive and tumor free for >5 yr since initial diagnosis; one was alive for >5 yr, and another for >4 yr from the start of treatment. Only mild and moderate toxicities were observed, which included three cases of **skin** allergy, two cases of anemia, fever and hypernatremia, and single cases of agranulocytosis, hypoglycemia, numbness, tiredness, myalgia and vomiting. The results compared favorably with the responses of patients treated with **radiation therapy** and chemotherapy.

IT **104624-98-8**, Antineoplaston AS2-1 **128932-52-5**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antineoplaston A10 and AS2-1 in patients with recurrent diffuse intrinsic brain stem glioma)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117979 HCAPLUS
DOCUMENT NUMBER: 138:165524
TITLE: New members of the transient receptor potential calcium channel family LTPRC3 including splice variants and cDNAs encoding them and their diagnostic and therapeutic uses
INVENTOR(S): Lee, Ning; Chen, Jian; Feder, John N.; Wu, Shujian; Lee, Liana; Blanar, Michael A.; Bol, David; Levesque, Paul C.; Sun, Lucy
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 508 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003012063	A2	20030213	WO 2002-US24445	20020801
WO 2003012063	A3	20040805		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1463814	A2	20041006	EP 2002-761217	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-309544P P 20010802
WO 2002-US24445 W 20020801

AB The present invention provides novel polynucleotides encoding LTRPC3 polypeptides, fragments and homologues thereof. The present invention also provides polynucleotides encoding variants and splice variants of LTRPC3 polypeptides, LTRPC3b, LTRPC3c, LTRPC3d, LTRPC3e, and LTRPC3f, resp. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention

further relates to diagnostic and therapeutic methods for applying these novel LTRPC3, LTRPC3b, LTRPC3c, LTRPC3d, LTRPC3e, and LTRPC3f polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

IT **497146-38-0 497146-76-6**
RL: PRP (Properties)
(unclaimed sequence; new members of the transient receptor potential calcium channel family LTPRC3 including splice variants and cDNAs encoding them and their diagnostic and therapeutic uses)

L24 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:933076 HCAPLUS
DOCUMENT NUMBER: 136:58537
TITLE: Nontoxic vernix compositions and method of producing
INVENTOR(S): Hoath, Steven B.; Pickens, William L.; Visscher, Martha O.
PATENT ASSIGNEE(S): Children's Hospital Medical Center, Philadelphia, USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 257,008.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6333041	B1	20011225	US 1999-447108	19991122
US 5989577	A	19991123	US 1998-33209	19980302
CA 2390767	AA	20010531	CA 2000-2390767	20001113
WO 2001037847	A2	20010531	WO 2000-US31059	20001113
WO 2001037847	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1231927	A2	20020821	EP 2000-978547	20001113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003514864	T2	20030422	JP 2001-539461	20001113
US 2002039590	A1	20020404	US 2001-850844	20010508
US 6562358	B2	20030513		
US 2003113355	A1	20030619	US 2002-241184	20020911
US 6846490	B2	20050125		

PRIORITY APPLN. INFO.:

US 1998-33209	A2	19980302
US 1999-257008	A2	19990225
US 1999-447108	A	19991122
US 2000-202567P	P	20000510
WO 2000-US31059	W	20001113
US 2001-850844	A3	20010508

AB A composition containing vernix to provide **therapeutic** treatment in a human, and a method for using the composition, are disclosed. The composition may

contain a natural or synthetic medicament, or may be manipulated to regulate transport properties. The medicament may be, for example, a protectant against UV **radiation** or an antioxidant. Various compns. and uses of vernix, both natural and synthetic, are disclosed. The compns. may be used in embodiments such as **skin** protection, wound healing, and restoration of epidermal barrier function. Photographs of a Western blot anal. demonstrating surfactant protein-A and protein-D in vernix. is depicted (no data).

IT **56-85-9**, Glutamine, biological studies
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nontoxic vernix compns. and method of producing)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:851786 HCAPLUS
DOCUMENT NUMBER: 136:4707
TITLE: Immunostimulatory nucleic acids for inducing a Th2 immune response
INVENTOR(S): McCluskie, Michael J.; Davis, Heather L.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001044416	A1	20011122	US 2001-768012	20010122
CA 2396871	AA	20011220	CA 2001-2396871	20010122
WO 2001095935	A1	20011220	WO 2001-US2170	20010122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1311288	A1	20030521	EP 2001-903236	20010122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: US 2000-177461P P 20000120
WO 2001-US2170 W 20010122

AB The invention relates to methods and products for inducing an immune response using immunostimulatory nucleic acids. In particular the immunostimulatory nucleic acids preferentially induce a Th2 immune response. The invention is useful for treating and preventing disorders associated with a Th1 immune response or for creating a Th2 environment for treating disorders that are sensitive to Th2 immune responses. These disorders include Th1-mediated disease, autoimmune disease, infection, and cancer.

IT **53678-77-6D**, Muramyl dipeptide, derivs. **66112-59-2**, SAF 1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vaccine comprising a Th2 immunostimulatory nucleic acid and/or an antigen and/or a therapeutic agent (cytokine, adjuvant, or drug) for treatment or prevention of various diseases)

L24 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:360798 HCAPLUS
DOCUMENT NUMBER: 135:251535
TITLE: Comparative evaluation of blood plasma and tumor **tissue** amino acid pool in **radiation** or neoadjuvant preoperative **therapies** of **breast** cancer with the antitumor drug Ukrain
AUTHOR(S): Nefyodov, L. I.; Uglyanitsa, K. N.; Smirnov, V. Y.; Karavay, A. V.; Brzosko, W.
CORPORATE SOURCE: Laboratory of Analytical Biochemistry, Institute of Biochemistry, National Academy of Sciences of Belarus, Grodno, 230017, Belarus
SOURCE: Drugs under Experimental and Clinical Research (2000), 26(5/6), 231-237
CODEN: DECRDP; ISSN: 0378-6501
PUBLISHER: Bioscience Ediprint Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study comparatively evaluated free amino acid pool formation in patients with T1-3NO-2MO **breast** cancer treated with the drug Ukrain (25 patients, i.v. 100 mg/course) in combination with preoperative **radiation** or neoadjuvant **therapies** (25 subjects, total dose 20 Gy). All the patients underwent radical mastectomy. Preoperative **radiation** did not essentially change the range of the blood plasma parameters studied. However, the authors observed decreased concns. of blood plasma ornithine and citrulline and a reduced content of aminobutyric acid, as compared with levels on admission, which may indicate an acceleration of detoxication processes in the liver. In comparison with healthy mammary gland **tissue**, the tumor **tissue** of the patients subjected to **radiation therapy** showed 1.5- to twofold increased concns. of cysteate, taurine, aspartate, glutamate, proline, glycine, alanine, valine, tyrosine and histidine, which substantiates the idea of tumor **tissue** being a trap for numerous energy and plastic substrates and indicates active transport of the above compds. into the tumor. The application of Ukrain had virtually no influence on concns. of the majority of blood plasma amino acids and derivs.: the total concentration of the compds. studied as well as the essential and nonessential amino acid pools remained unchanged. As compared with healthy **breast tissue**, the considerably increased levels of thiol-containing amino acids, such as methionine, cystine, cysteate and taurine, in the tumor **tissue** of patients receiving neoadjuvant **therapy** with Ukrain, indicates high activity of trans-sulfuration processes in this **tissue.** Simultaneously, in contrast to **radiation therapy**, Ukrain induced a marked dose-dependent increase in the concentration of proline in **breast** tumor **tissue.** The above changes were consistent with the results of the morphol. study which confirmed the emergence of numerous foci of necrosis in the tumor and indicated activation of Ukrain-induced proteolytic and degradation processes in the tumor. The results obtained have led the authors to conclude that a mechanism of Ukrain's cancerostatic effect is to control the transport and reactions of intermediate amino acid metabolism as well as to activate proline biosynthesis in the tumor, causing enhanced development of connective **tissue.** It is suggested that an important practical conclusion from the present study is the lack of

damaging effect of preoperative **radiation therapy** in the above regimen and the favorable (normalizing) action of Ukrain, at a course dose of 100 mg, on the amino acid pool formation in the organism of patients with **breast** cancer.

IT **56-85-9**, Glutamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(blood plasma and tumor **tissue** amino acid pool in **radiation** or neoadjuvant preoperative **therapies** of **breast** cancer with Ukrain in humans)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:735501 HCAPLUS
DOCUMENT NUMBER: 123:102786
TITLE: Modified platelet factor 4 (PF4) compositions and therapeutic and diagnostic use
INVENTOR(S): Maione, Theodore E.; Lai, Chee Kong
PATENT ASSIGNEE(S): Repligen Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9512414	A1	19950511	WO 1994-US12737		19941104
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9511717	A1	19950523	AU 1995-11717		19941104
PRIORITY APPLN. INFO.:			US 1993-149104	A	19931105
			WO 1994-US12737	W	19941104

AB The invention pertains to the use of modified PF4 to inhibit angiogenesis. The modified PF4 has utility for treating angiogenic diseases and for the inhibition of endothelial cell proliferation. Also, the invention concerns modifications of PF4 which extend the half-life and facilitate the targeting of the biol. activity of PF4 to specific locations. Furthermore, PF4 itself can be used to target the activities of other mols. to locations of angiogenesis and endothelial cell proliferation. Conjugation of recombinant PF4 (rPF4) with albumin, glycine Me ester, fluorescein derivs., PEG, etc. is described. Also described are construction and biol. activity of various mutant recombinant rPF4 mols. A PEG-rPF4 conjugate inhibited melanoma lung metastases. The PEG-rPF4 conjugate showed an advantageous clearance rate from the bloodstream, compared to rPF4.

IT **131571-32-9 136512-13-5 147035-44-7 147035-45-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(platelet factor 4 conjugates and therapeutic and diagnostic use)

IT **136512-13-5DP**, conjugates with fluorescein isothiocyanate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(platelet factor 4 conjugates and therapeutic and diagnostic use)

L24 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:16343 HCAPLUS
DOCUMENT NUMBER: 108:16343
TITLE: Antibody complexes of hapten-modified diagnostic or therapeutic agents
INVENTOR(S): Frincke, James M.; Meyer, Damon L.; David, Gary S.; Bartholomew, Richard M.
PATENT ASSIGNEE(S): Hybritech, Inc., USA
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 217577	A2	19870408	EP 1986-307031	19860912
EP 217577	A3	19870909		
EP 217577	B1	19920610		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1282069	A1	19910326	CA 1986-517663	19860908
AU 8662646	A1	19870319	AU 1986-62646	19860912
AU 597903	B2	19900614		
JP 62070377	A2	19870331	JP 1986-216963	19860912
AT 77056	E	19920615	AT 1986-307031	19860912
IL 80020	A1	19930114	IL 1986-80020	19860912
IL 97411	A1	19930114	IL 1986-97411	19860912
IL 97412	A1	19930404	IL 1986-97412	19860912
AU 9049750	A1	19901129	AU 1990-49750	19900213
AU 629903	B2	19921015		

PRIORITY APPLN. INFO.: US 1985-775461 A 19850912
EP 1986-307031 A 19860912
IL 1986-80020 A3 19860912

AB Hapten-modified diagnostic or **therapeutic** agents complexed with suitable anti-hapten antibodies are prepared which extend the serum half-life and permit an increased concentration of such diagnostic or **therapeutic** agents at in vivo target sites. 111In-bleomycin-Co-S-butane-linked EDTA conjugate (preparation given) 1-2 μCi and anti-hapten monoclonal antibody 0-100 μg were injected into mice. Tumor and organ uptake levels were measured 24 h after administration. The antibody enhanced tumor uptake, extended the serum lifetime, and altered the biodistribution of the drug. With antibody-mediated delivery, a higher percent dose of the hapten-modified pharmaceutical is concentrated at the tumor site and **radiation** reaching the site is enhanced. At low antibody concentration, the distribution is similar to the drug in the absence of antibody, whereas at high antibody concentration the drug distribution is similar to the antibody distribution.

IT **31362-50-2**, Bombesin
RL: BIOL (Biological study)
(chimeric antibodies to hapten-modified diagnostic or therapeutic agents and, serum half-life and target site concentration of agent increase with)

=> => file medline,biosis,embase
FILE 'MEDLINE' ENTERED AT 14:20:14 ON 13 APR 2005

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FILE 'BIOSIS' ENTERED AT 14:20:14 ON 13 APR 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 14:20:14 ON 13 APR 2005
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     (FILE 'HOME' ENTERED AT 13:53:53 ON 13 APR 2005)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:54:05 ON 13 APR 2005
               E GLUTAMINE
L1         48191 S E3

     FILE 'HCAPLUS' ENTERED AT 13:54:24 ON 13 APR 2005
L2         71817 S L1
               E RADATION
               E RADIATION
L3        669136 S E3
               E THERAPY
L4        257216 S E3
L5            56 S L2 AND L3 AND L4
               E SKIN/CT
L6        165796 S E3+ALL
               E BREAST
               E BREAST/CT
L7         59269 S E3+ALL
               E TISSUE/CT
L8         55161 S E3+ALL
L9             5 S L5 AND L6 AND L7 AND L8
               E KLINBERG S/AU
               E KLIMBERG S/AU
L10           27 S E4-E6
               E PETIT R/AU
L11           38 S E3
               E PETIT G/AU
L12           58 S E3,E13
               E SHINAL E,AU
               E SHINAL E/AU
L13           10 S E5
               E SHINAL C/AU
L14           11 S E4-E5
L15          133 S L10 OR L11 OR L12 OR L13 OR L14
L16            0 S L10 AND L11 AND L12 AND L13 AND L14
L17            1 S L5 AND L15
L18           67 S L2 AND (RADIATION (L) THERAP?)
L19           32 S L18 AND (SKIN OR BREAST OR TISSUE)
L21            3 S L18 AND L19 AND MUCOSAL
L22            0 S L18 AND (NON (L) MUCOSAL (L) TISSUE)
L23            0 S L19 AND (NON (L) MUCOSAL (L) TISSUE)
L24           15 S L18 AND (SKIN OR BREAST (L) TISSUE)

     FILE 'HCAPLUS' ENTERED AT 14:14:12 ON 13 APR 2005

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:15:30 ON 13 APR 2005
               E GLUTAMINE
L25        77118 S E3
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L26          963 S L25 AND (SKIN OR BREAST (L) TISSUE)
L***           0 S L*** AND RADIATION
L***           0 S L*** AND RADIATION
L***           0 S L*** AND RADIATION
L28            0 S L*** AND RADIATION
L29           28 S L26 AND RADIATION
L30            6 S L26 AND (RADIATION (L) THERAP?)

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:20:14 ON 13 APR 2005

=> d ibib abs l30 tot

L30  ANSWER 1 OF 6     MEDLINE on STN
ACCESSION NUMBER:    2003199457     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 12718563
TITLE:               Phase II study of antineoplaston A10 and AS2-1 in patients
                     with recurrent diffuse intrinsic brain stem glioma: a
                     preliminary report.
AUTHOR:              Burzynski Stanislaw R; Lewy Robert I; Weaver Robert A;
                     Axler Maxwell L; Janicki Tomasz J; Jurida Gabor F;
                     Paszkowiak Jaroslaw K; Szymkowski Barbara G; Khan Mohammad
                     I; Bestak Mark
CORPORATE SOURCE:    Department of Internal Medicine, Burzynski Clinic, Houston,
                     Texas, USA.. info@burzynskiclinic.com
SOURCE:              Drugs in R&D, (2003) 4 (2) 91-101.
                     Journal code: 100883647. ISSN: 1174-5886.
PUB. COUNTRY:        New Zealand
DOCUMENT TYPE:       (CLINICAL TRIAL)
                     (CLINICAL TRIAL, PHASE II)
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200311
ENTRY DATE:          Entered STN: 20030430
                     Last Updated on STN: 20031217
                     Entered Medline: 20031118
```

AB OBJECTIVE: A phase II study of antineoplaston A10 and AS2-1 was conducted to evaluate the antineoplastic activity in patients with recurrent diffuse intrinsic brain stem glioma. PATIENTS AND METHODS: This report describes the results of treatment of the first 12 patients admitted to the study. Patients received escalating doses of antineoplaston A10 and AS2-1 by intravenous bolus injections. The median duration of treatment was 6 months and the average dosage of antineoplaston A10 was 11.3 g/kg/day and of antineoplaston AS2-1 0.4 g/kg/day. Responses were assessed by gadolinium-enhanced magnetic resonance imaging of the head. RESULTS: Of ten evaluable patients, complete response was determined in two cases (20%), partial response in three (30%), stable disease in three (30%) and progressive disease in two (20%). Survival at 2 years was 33.3%. Currently, of all 12 patients, two (17%) were alive and tumour free for over 5 years since initial diagnosis; one was alive for more than 5 years, and another for more than 4 years from the start of treatment. Only mild and moderate toxicities were observed, which included three cases of **skin** allergy, two cases of anaemia, fever and hypernatraemia, and single cases of agranulocytosis, hypoglycaemia, numbness, tiredness, myalgia and vomiting. CONCLUSION: The results of this study compared favourably with the responses of patients treated with **radiation therapy** and chemotherapy. The study continues with accrual of additional patients.

L30 ANSWER 2 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004128591 EMBASE

TITLE: Post-irradiation approaches to treatment of radiation injuries in the context of radiological terrorism and radiation accidents: A review.

AUTHOR: Moulder J.E.

CORPORATE SOURCE: J.E. Moulder, Radiation Oncology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, United States. jmoulder@mcw.edu

SOURCE: International Journal of Radiation Biology, (2004) Vol. 80, No. 1, pp. 3-10.
Refs: 80
ISSN: 0955-3002 CODEN: IJRBA3

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 014 Radiology
017 Public Health, Social Medicine and Epidemiology
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20040412
Last Updated on STN: 20040412

AB Purpose: Events of the recent past have focused attention on the possibility of radiological (nuclear) terrorism and on the implications of such terrorist threats for radiation accident preparedness. This review discusses recent advances in the knowledge about how radiation injuries from such events might be treated pharmacologically, and the practical barriers to clinical utilization of these approaches. Conclusions: A wide range of pharmacological approaches are being developed in the laboratory that could greatly expand the ability to treat acute and chronic radiation injuries. However, there are currently a variety of practical and legal barriers that would prevent the actual clinical use of most of the approaches. There are also the potential weaknesses in most of the current programmes for dealing with the consequences of radiation accidents or nuclear terrorism, including the absence of widespread radiation biodosimetry capabilities and the resulting inability to triage. If a major radiation accident or terrorist event occurs, the lack of biodosimetry and treatment capabilities will be compounded by widespread public fear of 'radiation'.

L30 ANSWER 3 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003354167 EMBASE

TITLE: Phase II study of antineoplaston A10 and AS2-1 in patients with recurrent diffuse intrinsic brain stem glioma: A preliminary report.

AUTHOR: Burzynski S.R.; Lewy R.I.; Weaver R.A.; Axler M.L.; Janicki T.J.; Jurida G.F.; Paszkowiak J.K.; Szymkowski B.G.; Khan M.I.; Bestak M.

CORPORATE SOURCE: Dr. S.R. Burzynski, Burzynski Clinic, Department of Internal Medicine, 9432 Old Katy Road, Houston, TX, United States. info@burzynskiclinic.com

SOURCE: Drugs in R and D, (2003) Vol. 4, No. 2, pp. 91-101.
Refs: 41
ISSN: 1174-5886 CODEN: DRDDFD

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030918
Last Updated on STN: 20030918

AB Objective: A phase II study of antineoplaston A10 and AS2-1 was conducted to evaluate the antineoplastic activity in patients with recurrent diffuse intrinsic brain stem glioma. Patients and methods: This report describes the results of treatment of the first 12 patients admitted to the study. Patients received escalating doses of antineoplaston A10 and AS2-1 by intravenous bolus injections. The median duration of treatment was 6 months and the average dosage of antineoplaston A10 was 11.3 g/kg/day and of antineoplaston AS2-1 0.4 g/kg/day. Responses were assessed by gadolinium-enhanced magnetic resonance imaging of the head. Results: Of ten evaluable patients, complete response was determined in two cases (20%), partial response in three (30%), stable disease in three (30%) and progressive disease in two (20%). Survival at 2 years was 33.3%. Currently, of all 12 patients, two (17%) were alive and tumour free for over 5 years since initial diagnosis; one was alive for more than 5 years, and another for more than 4 years from the start of treatment. Only mild and moderate toxicities were observed, which included three cases of **skin** allergy, two cases of anaemia, fever and hypernatraemia, and single cases of agranulocytosis, hypoglycaemia, numbness, tiredness, myalgia and vomiting. Conclusion: The results of this study compared favourably with the responses of patients treated with **radiation therapy** and chemotherapy. The study continues with accrual of additional patients.

L30 ANSWER 4 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002227209 EMBASE
TITLE: Clinical applications of radioprotectors.
AUTHOR: Werner-Wasik M.
CORPORATE SOURCE: M. Werner-Wasik, Department of Radiation Oncology, Kimmel Cancer Center, Jefferson Medical College, 11 South 11th Street, Philadelphia, PA 19107, United States. maria.werner-wasik@mail.tju.edu
SOURCE: Expert Review of Anticancer Therapy, (2001) Vol. 1, No. 2, pp. 309-316.
Refs: 34
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020711
Last Updated on STN: 20020711

AB Patients with malignant or benign tumors who receive **radiation**

therapy - frequently in combination with chemotherapy - are likely to experience side effects, either acutely or chronically. After several decades of preclinical and clinical research efforts, a first approved radioprotective drug, amifostine, has been introduced into the clinic. Although thus far it has been demonstrated to be effective only for the prevention of dry mouth following radiotherapy, it has the potential to be applied in many other oncologic situations.

L30 ANSWER 5 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002129978 EMBASE
TITLE: Radiation damage to the rectum and anus: Pathophysiology, clinical features and surgical implications.
AUTHOR: Reis E.D.; Vine A.J.; Heimann T.
CORPORATE SOURCE: E.D. Reis, Department of Surgery, The Mount Sinai Medical Centre, One Gustave L. Levy Place, New York, NY 10029-6574, United States. emane.reis@mountsinai.org
SOURCE: Colorectal Disease, (2002) Vol. 4, No. 1, pp. 2-12.
Refs: 93
ISSN: 1462-8910 CODEN: CODIFU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 014 Radiology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020425
Last Updated on STN: 20020425

AB **Radiation** kills cancer cells by inducing various degrees of deoxyribonucleic acid fragmentation and disruption of intracellular membranes that lead to either immediate or delayed cell death. Although **radiation** can be effective in destroying cancer, its usefulness is limited by damage to normal tissues that surround the target tumour or those in the path of the **radiation** beam. The rectum and anus are damaged frequently during radiotherapy for abdominopelvic malignancy, including preresection **therapy** for rectal cancer. Such damage is often associated with lesions in the perineal **skin**, genitourinary tract, colon, and small intestine. Surgical intervention often is required for the most severe forms of these complications.

L30 ANSWER 6 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 80000591 EMBASE
DOCUMENT NUMBER: 1980000591
TITLE: Effects of methionine sulfoximine analogs on the synthesis of **glutamine** and glutathione: Possible chemotherapeutic implications.
AUTHOR: Meister A.; Griffith O.W.
CORPORATE SOURCE: Dept. Biochem., Cornell Univ. Med. Coll., New York, N.Y. 10021, United States
SOURCE: Cancer Treatment Reports, (1979) Vol. 63, No. 6, pp. 1115-1121.
CODEN: CTRRDO
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index

016 Cancer
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB Methionine sulfoximine inhibits the synthesis of **glutamine**, and also, by virtue of its inhibition of γ-glutamylcysteine synthetase, the synthesis of glutathione. The studies presented in this paper on methionine sulfoximine and its analogs have potential chemotherapeutic interest because there is evidence that depletion of a specific amino acid (e.g., asparagine or **glutamine**) may have beneficial **therapeutic** effects, and certain tumors (e.g., those of the liver, **skin**, and colon) exhibit high levels of γ-glutamyl transpeptidase, the enzyme that catalyzes the degradation of glutathione according to the γ-glutamyl cycle. Some tumors have high levels of glutathione, and both glutathione levels and γ-glutamyl transpeptidase activities are reported to be increased in tumors, as well as after administration of carcinogens. Inhibition of the γ-glutamyl cycle, which has been postulated to play a role in the transport of amino acids, may reduce amino acid transport into certain tumors. Depletion of glutathione might make tumors more susceptible to **radiation** or chemotherapeutic agents. The γ-glutamyl derivatives of some chemotherapeutic agents might be transported into certain tumors more readily than the free agents. Specific inhibitors of the individual reactions of the γ-glutamyl cycle have been obtained. Substrate analogs have been found that function in some but not all of the reactions. Methionine sulfoximine inhibits **glutamine** synthetase and γ-glutamylcysteine synthetase irreversibly by forming enzyme-bound methionine sulfoximine phosphate. An understanding of the mechanisms of action of these enzymes and a knowledge of the topology of their active sites have led to the synthesis of two highly selective sulfoximine inhibitors. Thus, α-ethylmethionine sulfoximine was prepared and was found to inhibit **glutamine** synthetase in vitro and in vivo, but was also found to be essentially inactive toward γ-glutamylcysteine synthetase. Administration of α-ethylmethionine sulfoximine leads to substantial decreases in tissue **glutamine** levels without affecting glutathione levels appreciably. Studies on the mapping of the active sites of the two synthetases led to the prediction that substitution of bulkier alkyl groups for the S-methyl group of methionine sulfoximine would yield a selective inhibitor of γ-glutamylcysteine synthetase. This prediction was fulfilled by the finding that prothionine sulfoximine (S-n-propyl homocysteine sulfoximine) is an excellent inhibitor of γ-glutamylcysteine synthetase and only a very weak inhibitor of **glutamine** synthetase. It has thus been possible, by suitable structural modification, to direct an inhibitor to one enzyme in preference to another very similar enzyme, despite the fact that both enzymes act by closely analogous mechanisms involving formation of the same enzyme-bound intermediate. This approach might be usefully applied to other powerful enzyme inhibitors such as azaserine or 6-diazo-5-oxo-L-norleucine, and thus might provide reagents that would inhibit specific enzyme targets.